DEPARTMENT OF HEALTH AND HUMAN SERVICE

HFI-35

Public Health Service

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Food and Drug Administration
New Orleans District
Southeast Region
6600 Plaza Drive, Suite 400
New Orleans, LA 70127

Telephone: 504-240-4500
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signed by CSO

September 21, 1999

WARNING LETTER NO. 99-NOL-44

FEDERAL EXPRESS
OVERNITE DILIVERY

Mr. Glenn A. Pruitt, President
PharmaScience Laboratories, LLC
136 Weisenberger Road, Suite B
Madison, Mississippi 39110

Dear Mr. Pruitt:

On September 1, 1999 through September 20, 1999, the U.S. Food and Drug Administration conducted and inspection of your facility located in Madison, Mississippi. Our investigators determined that your firm repackages and relabels prescription drugs. The products you repackage and relabel are drug products as defined by Section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act). The above stated inspection revealed that your products are adulterated within the meaning of Section 501(a)(2)(B) of the Act in that the controls used for the manufacturing, processing, packaging or holding of these products are not in conformance with current Good Manufacturing Practice regulations under Title 21, Code of Federal Regulations (CFR), Parts 210 and 211. Deviations noted during the inspection include, but are not limited to, the following:

1. Failure to maintain original records covering the repackaging of drug samples, as required by Title 21, CFR, Part 211.180(c). For example, three of seven completed batch records and one of four in-process records contained discrepancies. These included records being signed and dated by personnel before they were employed by the firm; one lot of product for which no batch record for re-packaging was available; and, shipping records for finished product being shipped before its recorded repackaged date;

2. Failure to have a written procedure for the issuance and reconciliation of labeling as required by Title 21, CFR, Part 211.125. For example, the roll label verification does not support the number of labels issued for [redacted]

3. Failure to establish a written procedure which addresses the receipt, storage, review, and release of labeling, as required by Title 21, CFR, Part 211.122. For example, the firm had

no documentation of approval or rejection of labeling and all labels were stored in open warehouse in unlocked cabinet;

4. Failure to establish acceptance criteria for actual yield for all lots of products, as required by Title 21, CFR, Part 211.103. For example, determination of the actual yield and the percentage of theoretical yield were not performed at the conclusion of each phase of processing and packaging but at the conclusion of repackaging, a procedure which sometimes may take up to six (6) months to complete;

5. Failure of repackaged drug products to bear expiration dates determined by appropriate stability studies to assure these drug products meet appropriate standards of identity, strength, quality, and purity at time of use, as required by Title 21, CFR, Part 211.137. For example, you have not established a written stability testing program;

6. Failure to establish a written procedure describing the receipt, identification, storage, handling, sampling, testing, and release of components and drug products for repackaging, as required by Title 21, CFR, Part 211.80. For example, a damaged container of bottle caps was exposed to warehouse environmental conditions;

7. Failure to determine that container closure systems shall provide adequate protection against external factors during storage and use, as required by Title 21, CFR, Part 211.94(b). For example, some of your liquid products are packaged in clear containers instead of light resistant ones, as specified by the manufacturer's and your label requirements;

8. Failure to test and approve or reject containers, closures, and bulk products before release for use, as required by Title 21, CFR, Part 211.84. For example, the status (quarantined, approved, or rejected) was not recorded on stored containers, closures, and bulk products;

9. Failure to visually examine bulk products, containers and closures for appropriate labeling, container damage, broken seals, and approval or rejection by the Quality Control unit before use, as required by Title 21, CFR, Part 211.82. For example, two opened bulk containers identified as "Contaminated" and containing loose tablets were stored on the same pallet with intact containers of bulk product;

10. Failure to implement appropriate controls to ensure the prevention of mix-ups and cross contamination by physical and spatial separation from operations on other drug products, as required by Title 21, CFR, Part 211.130(a). For example, on September 1, 1999, while the repackaging of [redacted] tablets was in progress, our investigators observed an unlabeled container of [redacted] tablets in the same room only a few feet away from the repackaging operation;

11. Failure to have and follow a written procedure for cleaning and maintenance of the repackaging equipment, as required by Title 21, CFR, Part 211.67. For example, cleaning procedure for the [redacted] liquid filling machine and the [redacted] tablet machine has not been validated;

12. Failure to have a written procedure for the preparation of Master Production Records, as required by Title 21, CFR, Part 211.186(a). For example, Master Production Records lack: 1) name and weight of each active ingredient; 2) list of containers, closures and packaging materials to ensure they meet predetermined specifications; 3) copy of labeling; and, 4) percent theoretical yield;

13. Failure to have a written procedure for the preparation of Batch Records, as required by Title 21, CFR, Part 211.188. For example, Batch Records lack: 1) name of person who performed operation and date on which it was performed; 2) documentation of bulk product and labeling utilized; and, 3) documentation of examination of packaging and labeling material for correctness prior to packaging;

14. Failure to ensure that each person engaged in the manufacturing, processing, packing, or holding of a drug product has the education, training, and experience to enable that person to perform the assigned task, as required by Title 21, CFR, Part 211.25. For example, the production manager performed training of all personnel from April 27, 1999 to present, in spite of the fact that he hadn't received any CGMP training until July 14,1999, and no training records were available for the high school students who work part time at the firm;

15. Failure to have adequate space to prevent mix-ups and contamination of drug products, as required by Title 21, CFR, Part 211.42(c). For example, unlabeled totes of [redacted]blets were located in the same room tha[redacted]tablets were being repackaged;

16. Failure to have a written procedure for the prevention of microorganisms, as required by Title 21, CFR, Part 211.113. For example, liquid filling room employees do not wear protective gear to protect exposed product from mouth and/or nasal discharge and a mold-like substance was observed on the ceiling above an area where liquid products are processed;

17. Failure to have a written procedure for the calibration of instruments, apparatus, gauges, and recording devices at suitable intervals, as required by Title 21, CFR, Part 211.160(b)(4);

18. Failure to have a written procedure to cover retesting of approved components, drug product containers and closures after exposure to conditions that might adversely effect the product, as required by Title 21, CFR, Part 211.87. For example, racks of bottles used for filling liquid product were left uncapped overnight in the filling room. Each rack of bottles was covered with a clear plastic cover that did not protect the bottles from contamination;

19. Failure to validate all of the equipment utilized in repackaging for all products, as required by Title 21, CFR, Part 211.68;

20. Failure to complete all review of repackaging procedure before release of product, as required by Title 21, CFR, Part 211.165. For example, partial batches of product are

routinely released and distributed for sale before calculations of yield, label reconciliation, and review and approval by the Quality Assurance unit have been completed;

21. Failure to investigate an out of specification product yield, as required by Title 21, CFR, Part 211.103. For example, you failed to investigate a 113% product yield for [redacted] lot # [redacted] in spite of the fact that it was outside of the 90-110% specification;

22. Failure to retain a representative reserve sample for all products, as required by Title 21, CFR, Part 211.170(a). For example, you do not have a valid procedure for obtaining reserve samples that are representative of the entire production run;

23. Failure to have a written procedure stating the responsibilities of the quality control unit, as required by Title 21, CFR, Part 211.22(d); and,

24. Failure to have records available for inspection, as required by Title 21, CFR, Part 211.180(c). For example, the following Batch Records were not available when requested by FDA: [redacted] numbers [redacted] and [redacted] lot numbers [redacted] and [redacted] lot number [redacted] lot number [redacted] and [redacted] numbers [redacted] and [redacted].

One of our primary areas of concern is the lack of adequate stability studies to support expiration dates used on each repackaged drug product for each container type. Under certain conditions the original bulk drug manufacturer's expiration date may be used without conducting stability studies. However, all conditions must be met. These conditions can be found in the "Draft Guideline on Repackaging of Solid Oral Dosage Form Drug Products." We have enclosed a copy for your review.

Examples of conditions which must be met are:

A. The original bulk container of drug product was not opened previously and the entire contents are repackaged in one operation;
B. The original bulk drug manufacturer's container was other than glass and the repackaging container was demonstrated to be equivalent to or exceed the original bulk manufacturer's container in terms of water vapor permeation and compatibility with the drug product, or where the original bulk drug manufacturer's container is polyethylene, and the repackaging container meets current USP standards for high density polyethylene containers;
C. The repackaging container either meets or exceeds the original bulk manufacturer's container specification for light transmission or meets the current USP standard for light transmission;
D. The repackaging container meets or exceeds the special protective feature of the original bulk manufacturer's container, e.g., for material leaching and low moisture; and,
E. The repackaging container-closure system meets current USP standards for a "tight container" or a "well-closed container".

Because your firm does not appear to meet the above conditions "A" through "E", you must conduct adequate stability studies to support expiration dates used on all repackaged drug products.

The violations identified in this letter are not intended to be an all-inclusive list of deficiencies at your facility. You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action, including seizure or injunction, without further notice. Federal agencies are advised of the issuance of all warning letters for drug products so that they may take this information into account when considering the award of contracts.

Please advise this office, in writing, within fifteen (15) working days after receipt of this letter, of the specific actions you have taken to correct the violations. Your response should include: 1) each step that has been taken to completely correct the current violation and prevent its recurrence; 2) the time when corrections will be completed; and, 3) any documentation necessary to indicate corrections have been made.

If you have any additional questions, please feel free to call Ms. Carolyn S. Olsen at (504) 240-4519 or write to her at U.S. Food and Drug Administration, 6600 Plaza Drive, Suite 400, New Orleans, Louisiana 70127.

Sincerely,

James E. Gamet
District Director
New Orleans District

Enclosure: Form FDA 483
Guideline on Repackaging of Solid Oral Dosage Form Drug Products